

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Dyrberg et al.

Serial No.: To Be Assigned

Group Art Unit: To Be Assigned

Filed: May 2, 2001

Examiner: To Be Assigned

For: Prevention of A Disease Having The Characteristics of Diabetes

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

Before the above-captioned application is taken up for examination, entry of the following amendment is respectfully requested:

**IN THE SPECIFICATION:**

At page 1, before the first line, insert

**--CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a divisional of USSN 09/319,138 filed 19 December 1997, which is a 35 U.S.C. 371 national application of PCT/DK96/00297 filed July 1, 1996 and claims priority under 35 U.S.C. 119 of Danish application 0765/95 filed June 30, 1995, the contents of which are fully incorporated herein by reference.--

**IN THE CLAIMS:**

Please substitute the attached annexes to the International Preliminary Examination Report for pages 23-24 of the published PCT application WO 97/02043.

Cancel claims 1-5 and 7;

Substitute the following amended claim for the pending claim having the same claim number:

6. (Amended) A pharmaceutical composition for treating or ameliorating type 1 diabetes comprising a hormonally inactive insulin analogue selected from the group consisting of desA1 human insulin, des(A1-A2) human insulin, des(A1-A3) human insulin, desA21 human insulin, des(B1-B5) human insulin, des(B1-B6) human insulin, des(B24-B30) human insulin, des(B25-B30) human insulin, Gly<sup>A2</sup> human insulin, Ala<sup>A2</sup> human insulin, Nle<sup>A2</sup> human insulin, Thr<sup>A2</sup> human insulin, Pro<sup>A2</sup> human insulin, D-allo Ile<sup>A2</sup> human insulin, Nva<sup>A3</sup> human insulin, Nle<sup>A3</sup> human insulin, Leu<sup>A3</sup> human insulin, Val<sup>A2</sup>, Ile<sup>A3</sup> human insulin, Abu<sup>A2</sup>, Abu<sup>A3</sup> human insulin, Gly<sup>A2</sup>, Gly<sup>A3</sup> human insulin, D-Cys<sup>A6</sup> human insulin, D-Cys<sup>A6</sup>, D-Cys<sup>A11</sup> human insulin, Ser<sup>A6</sup>, Ser<sup>A11</sup>, des(A8-A10) human insulin, D-Cys<sup>A7</sup> human insulin, D-Cys<sup>A11</sup> human insulin, Leu<sup>A19</sup> human insulin, Gly<sup>B6</sup> human insulin, Glu<sup>B12</sup> human insulin, Asn<sup>B12</sup> human insulin, Phe<sup>B12</sup> human insulin, D-Ala<sup>B12</sup> human insulin, and Asp<sup>B25</sup> human insulin.

Please add the following new claims:

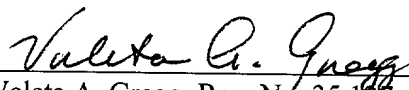
8. The pharmaceutical composition of claim 6, wherein the *in vitro* activity of the insulin analogue is less than 7% of the activity of human insulin.
9. The pharmaceutical composition of claim 6, wherein the insulin analogue is Asp<sup>B25</sup> human insulin.
10. The pharmaceutical composition of claim 6, wherein the mammal is a human being.

## REMARKS

This amendment is provided to amend the specification to recite the relationship of this divisional application to previously filed applications, and to add claims to the patentable subject pursued in this application. No new matter is presented, and the Examiner is kindly requested to enter this amendment.

Respectfully submitted,

Date: 2 May 2001

  
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**Marked Version Showing Changes Made**

6. (Amended) A pharmaceutical composition for [preventing or delaying the onset of a disease having the characteristics of] treating or ameliorating type 1 diabetes [or for ameliorating an early stage thereof in a mammal at risk of developing said disease which composition comprises an effective amount of a hormonally inactive insulin or insulin analogue according to any one of the claims 1 and 2 to 5] comprising a hormonally inactive insulin analogue selected from the group consisting of desA1 human insulin, des(A1-A2) human insulin, des(A1-A3) human insulin, desA21 human insulin, des(B1-B5) human insulin, des(B1-B6) human insulin, des(B24-B30) human insulin, des(B25-B30) human insulin, Gly<sup>A2</sup> human insulin, Ala<sup>A2</sup> human insulin, Nle<sup>A2</sup> human insulin, Thr<sup>A2</sup> human insulin, Pro<sup>A2</sup> human insulin, D-allo Ile<sup>A2</sup> human insulin, Nva<sup>A3</sup> human insulin, Nle<sup>A3</sup> human insulin, Leu<sup>A3</sup> human insulin, Val<sup>A2</sup>, Ile<sup>A3</sup> human insulin, Abu<sup>A2</sup>, Abu<sup>A3</sup> human insulin, Gly<sup>A2</sup>, Gly<sup>A3</sup> human insulin, D-Cys<sup>A6</sup> human insulin, D-Cys<sup>A6</sup>, D-Cys<sup>A11</sup> human insulin, Ser<sup>A6</sup>, Ser<sup>A11</sup>, des(A8-A10) human insulin, D-Cys<sup>A7</sup> human insulin, D-Cys<sup>A11</sup> human insulin, Leu<sup>A19</sup> human insulin, Gly<sup>B6</sup> human insulin, Glu<sup>B12</sup> human insulin, Asn<sup>B12</sup> human insulin, Phe<sup>B12</sup> human insulin, D-Ala<sup>B12</sup> human insulin, and Asp<sup>B25</sup> human insulin.

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